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EPA R.E.D. FACTS

IPRODIONE

Pesticide Reregistration

All pesticides sold or distributed in the United States must be registered by EPA, based on scientific studies showing that they can be used without posing unreasonable risks to people or the environment. Because of advances in scientific knowledge, the law requires that pesticides which were first registered before November 1, 1984, be reregistered to ensure that they meet today's more stringent standards.

In evaluating pesticides for reregistration, EPA obtains and reviews a complete set of studies from pesticide producers, describing the human health and environmental effects of each pesticide. The Agency develops any mitigation measures or regulatory controls needed to effectively reduce each pesticide's risks. EPA then reregisters pesticides that can be used without posing unreasonable risks to human health or the environment.

When a pesticide is eligible for reregistration, EPA explains the basis for its decision in a Reregistration Eligibility Decision (RED) document. This fact sheet summarizes the information in the RED document for reregistration case 2335, iprodione [3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide].

Use Profile

Iprodione is a contact and/or locally systemic fungicide registered for use on a variety of field, fruit, and vegetable crops, including almonds, grapes, peaches, potatoes, rice, berries, onions, peanuts, lettuce, golf courses, lawns, and ornamentals. There are currently 70 tolerances for iprodione. These end-use patterns for the current formulations have been classified for outdoor use only, applications include aircraft (fixed-wing and helicopter), airblast sprayer, chemigation, groundboom, high- and low-pressure handwand, backpack sprayer, and tractor-drawn spreader. Iprodione is formulated as a liquid, dry flowable, wettable powder, and granular.

Regulatory History

Iprodione was first registered in the U.S. in 1979 as a fungicide. Rhone-Poulenc Ag Co., is the current manufacturer of iprodione. A data call-in was issued in September 1991. Currently, 21 iprodione products are registered,

along with 18 Special Local Needs registrations (SLNs). Product concentrations range from 1.5% active ingredient to 95% active ingredient.

Human Health Assessment

Toxicity

In studies using laboratory animals, iprodione generally has been shown to be of low acute toxicity. It is slightly toxic by the eye, dermal and oral routes and has been placed in Toxicity Category III (the second lowest of four categories) for these effects. In acute inhalation and as a dermal sensitizer, iprodione is practically non-toxic (Category IV).

Iprodione was not mutagenic in several studies. Iprodione has been classified as a Group B2, or "likely," human carcinogen, based on evidence of tumors in both sexes of mouse (liver) and in the male rat (Leydig cell). A Q* of 4.39 x 10^{-2} was used for estimating carcinogenic risk (Leydig cell).

The endpoints selected for both the acute (decreased anogenital distance (AGD)) and the chronic (histopathology of male reproductive system) risk assessments are based on developmental and reproductive effects. It was determined that the additional 10x Safety Factor for the protection of infants and children (as required) by FQPA should be reduced to 3x and the rationale for reducing the 10x factor to 3x are as follows: no enhanced susceptibility was seen in rat and rabbit developmental and the two generation reproduction study in rats; the critical endpoint for acute dietary risk assessment (decreased AGD) was seen at a high dose (120 mg/kg/day) and there were only marginal differences in the degree of decreased AGD between the doses 20 mg/kg/day, 120 mg/kg/day, and 250 mg/kg/day thus indicating the "true" NOEL could be higher than the one established at 20 mg/kg/day; the proposed mode of action of iprodione is disruption of testosterone biosynthesis; the use of a realistic dietary exposure data (refined using monitoring data and percent crop treated).

The Agency used the developmental NOEL of 20 mg/kg/day based on AGD in male fetuses to assess acute dietary risk. The acute reference dose (RfD) for iprodione is 0.06 mg/kg/day. The Agency used the toxicity/carcinogenicity NOEL of 6.1 mg/kg/day to assess the chronic dietary risk for iprodione based on histopathological lesions in the male reproductive system and effects of the adrenal glands. The chronic RfD for iprodione is 0.02/kg/day.

Iprodione is structurally related to vinclozolin and procymidone. Each of these three pesticides can metabolize to 3,5-dichloroaniline (3,5-DCA). FQPA requires EPA to estimate cumulative risk from consumption of food and water containing 3,5-DCA derived from iprodione, vinclozolin, and procymidone. A

Q* of 6.38 X 10^{-2} (mg/kg/day) in human equivalents has been calculated for p-chloroaniline. This Q* is based on the spleen sarcoma rate in male rats from a bioassay study, linearized low-dose multistage model, and the 3/4s interspecies scaling factor.

Dietary Exposure

People may be exposed to residues of iprodione through the diet and drinking water. Tolerances were reassessed for iprodione and have been established in 40 CFR 180.399 for the following commodities: almonds, hulls; almonds, nutmeat; apricots; beans, dried, vine hay; beans, dry; beans, forage; beans, succulent; blueberries; boysenberries; broccoli; caneberries; carrots; cherries (sour); cherries (sweet); Chinese mustard; currants; garlic; ginseng; grapes; kiwi fruit; lettuce; nectarines; onions, dry bulb; peaches; peanuts; peanut forage; peanut hay; plums; potatoes; prunes; raspberries; rice grain; rice straw; strawberries; cattle, fat, kidney, liver, meat, meat byproducts; eggs; goats, fat, kidney, liver, meat, meat byproduct; hogs, fat, kidney, liver, meat, meat byproduct, horses, fat, kidney, liver, meat, meat byproduct; milk; poultry, fat, liver, meat, meat byproduct; and, sheep, fat, kidney, liver, meat, meat byproduct.

Occupational and Residential Exposure

Handlers (mixers, loaders, and applicators) of iprodione may be exposed to iprodione during and after normal use of liquid, wettable powder, dry flowable, and granular formulations. For dermal exposure, no short- and intermediate-term dermal risk for iprodione. For inhalation exposure, the current use of iprodione does not indicate a concern for long-term exposure or risk. Based on the use patterns and potential exposures, nineteen exposure scenarios for handlers were identified and assessed for iprodione. Rhone-Poulenc has voluntarily canceled all residential uses of iprodione.

Human Risk Assessment

The Agency was concerned about the cancer risk and the acute dietary risk posed by exposure to iprodione. The target Margin of Exposure (MOE) for acute dietary risk is 300; MOEs above 300 are not considered to be of concern. Acute MOEs for iprodione are calculated for females 13+ only, as discussed previously. With risk mitigation measures in place, the MOE for the

acute risk from food and drinking water for iprodione is 351, which the Agency considers acceptable.

Aggregate cancer risk from iprodione (from dietary, residential and water exposure) with risk mitigation measures in place is 1.8 x 10^{-6}, which is within the range that the Agency currently considers acceptable.

With personal protective equipment (PPE) in place, risk to handlers of iprodione are considered acceptable. The Agency has also determined that a restricted-entry interval (REI) of 24-hours reduces the post-application risks posed by iprodione to workers.

The cumulative carcinogenic risk estimate for consumption of food and wine containing residues of 3,5-DCA as a result of use of iprodione, vinclozolin, and procymidone is 9.5 X 10^{-7}.

Environmental Assessment

Environmental Fate

The major routes of dissipation are hydrolysis in neutral and alkaline environments (half-life pH 7 = 4.7 days; pH 9 = 27 minutes) and microbial degradation under both aerobic and anaerobic conditions. The overall result of these mechanisms of dissipation appears to indicate that iprodione has low to intermediate persistence in the environment. The results obtained in the field confirm the expected low persistence of iprodione ($t_{1/2}$ = 3-7 days).

Despite the fact that iprodione is mobile to highly mobile in some soils, it is unlikely that it will leach to ground water because of its rapid degradation in the environment. In addition, because iprodione is typically applied as a foliar treatment, degradation/metabolism on the plant surface and/or absorption by plants will further mitigate the potential for ground water contamination.

Ecological Effects

For acute exposure, iprodione is practically nontoxic to slightly toxic to birds, practically nontoxic to small mammals, relatively nontoxic to bees, moderately toxic to freshwater fish, moderately toxic to estuarine and marine fish, and moderately to highly toxic to estuarine and marine invertebrates. Chronic toxicity studies established the following No Observable Effect Concentration (NOEC) values and ecological endpoints affected: 300 ppm for birds (decreased hatchling body weight), 500 ppm for small mammals (decreased fetal weight); > 0.26 ppm for freshwater fish (larval survival);

> 0.17 ppm for freshwater invertebrates (offspring/female, mean percentage survival, growth); > 3.5 ppb for estuarine and marine invertebrates (offspring/female/reproductive day).

Ecological Effects Risk Assessment

EPA is generally concerned about the ecological effects to terrestrial wildlife and aquatic organisms posed by exposure to iprodione. The risk assessment for iprodione shows various levels of concern regarding avian risk and mammalian risk from broadcast applications of granular and nongranular products used on turf and ornamentals. In addition, most agricultural uses present acute and chronic risks of varying levels to endangered and nonendangered aquatic organisms, with turf and rice demonstrating the higher risks. In general, the risks to invertebrates are greater than the risks to fish. The turf and rice uses present high acute risks for nonvascular aquatic plants. With risk mitigation measures in place, the Agency considers these risks acceptable.

Risk Mitigation

To lessen human health risk, residential risk, worker risk, and ecological effects posed by iprodione, Rhone-Poulenc has requested changes to its iprodione registrations, including the following mitigation measures.

- For iprodione use on strawberries, increase the pre-harvest interval from 0-days to up to but not after first flower. In addition, the tolerance for strawberries will be reduced to the limit of quantitation (0.05 ppm).
- For iprodione use on all stone fruit (apricots, cherries, nectarines, plums, and prunes), increase the pre-harvest interval from 7-days to up to but not after petal fall (approximately 45 - 90-day pre-harvest interval). In addition, the tolerances for all stone fruit, including peaches, will be reduced to limit of quantitation (0.05 ppm).
- For iprodione use on table grapes (fresh, cooked, canned, juice, raisin or otherwise; mitigation does *not* include wine and sherry grapes), reduce the application rate from 4 times per season to one application per season at early- to mid-bloom. Tolerances remain unchanged consistent with the RED (10 ppm).
- Cancellation by Rhone-Poulenc of all residential uses of iprodione.
- Limit the maximum number of applications on non-residential turf, lawn, golf course, ornamental trees, and ornamental plants from “unlimited” to 6

per year, with the maximum annual application of up to but no more than 24 lbs. a.i..

- Except for use of iprodione on golf courses, include label warnings requiring a vegetative buffer strip of at least 25-feet for application of iprodione adjacent to water bodies such as lakes, reservoirs, rivers, permanent streams, marshes or natural ponds, estuaries, and commercial fish ponds.
- For use on golf courses, the following statement will be included on the label: “for golf courses only, do not apply to turf cut higher than 1" on golf holes where water bodies are present.”
- Include label warnings to prevent application of iprodione when wind direction is toward aquatic area.
- Cancellation by Rhone-Poulenc of all herbaceous ornamental seed treatment uses.
- All wettable powder formulations must be packaged in water-soluable bags.
- For rice use only, continue to include endangered species restrictions in the state of Arkansas (for the fat pocketbook pearly mussel and its habitat).

Additionally, there are a number of risk mitigation measures required in the RED to protect mixers, loaders, applicators and workers. For a detailed list, refer to Chapter IV of the Iprodione RED document. With the above mitigation measures, and the agreed upon changes to labels by Rhone-Poulenc, all uses of iprodione are eligible for reregistration.

Additional Data Required

The generic data base supporting the reregistration of iprodione for the above eligible uses has been reviewed and determined to be substantially complete. For confirmatory purposes, the following information is being required:

- Pre and/or Post-Natal Exposure Study *[GLN 83-3(a)]*;
- UV/Visible Absorption *[OPPTS 870.7050];*
- Density *[GLN 63-7]*;
- Product Chemistry Reports *[GLN 61/62]*;
- Aquatic Plant Growth Study *[GLN 122-2]*;
- Aerobic Soil Metabolism *[GLN 162-1]*;
- Leach/Adsorp/Desorption *[163-1]*;
- Confined Rotational Crop Study *[165-1]*;

- Estimation of Dermal/Inhalation Exposure *[GLN 231/232]*;
- Residue Analytical Methods *[GLN 171-4(d)]*;
- Crop Field Trial Studies (strawberries, stone fruit) *[GLN 171-4(k)]*;
- Surface Water Monitoring Study *[Special Study]*;

Product Labeling Changes Required

All iprodione end-use products must comply with EPA's current pesticide product labeling requirements and with those labeling requirements imposed in the Iprodione RED. For a comprehensive list of labeling requirements, please see section V of the Iprodione RED document.

Regulatory Conclusion

The Agency has determined that existing uses of iprodione are eligible for reregistration subject to conditions imposed in the RED. These include removal of all residential uses of iprodione (residential turf, residential ornamentals and residential vegetable/small fruit gardens) from product registrations due to cancer risk concerns. Also, to protect handlers of granular iprodione products, removal of belly grinder application method from iprodione product registrations. Lastly, to mitigate risks to birds, removal of herbaceous ornamental seed treatment from all iprodione registrations. Rhone-Poulenc has already requested these changes to its iprodione registrations. All other uses of iprodione are eligible for reregistration.

For More Information

EPA is requesting public comments on the Reregistration Eligibility Decision (RED) document for iprodione during a 60-day time period, as announced in a Notice of Availability published in the Federal Register. To obtain a copy of the RED document or to submit written comments, please contact the Pesticide Docket, Public Response and Program Resources Branch, Field Operations Division (7506C), Office of Pesticide Programs (OPP), US EPA, Washington, DC 20460, telephone 703-305-5805.

Electronic copies of the RED and this fact sheet are available on the Internet. See http://www.epa.gov/REDs.

Printed copies of the RED and fact sheet can be obtained from EPA's National Center for Environmental Publications and Information (EPA/NCEPI), PO Box 42419, Cincinnati, OH 45242-0419, telephone 513-489-8190, fax 513-489-8695.

Following the comment period, the Iprodione RED document also will be available from the National Technical Information Service (NTIS), 5285 Port Royal Road, Springfield, VA 22161, telephone 703-487-4650.

For more information about EPA's pesticide reregistration program, the Iprodione RED, or reregistration of individual products containing iprodione, please contact the Special Review and Reregistration Division (7508C), OPP, US EPA, Washington, DC 20460, telephone 703-308-8000. For information about the health effects of pesticides, or for assistance in recognizing and managing pesticide poisoning symptoms, please contact the National Pesticides Telecommunications Network (NPTN). Call toll-free 1-800-858-7378, between 9:30 am and 7:30 pm Eastern Standard Time, Monday through Friday.